REMARKS

In the present communication, claim 1 has been amended; claims 9 and 10 have been canceled without prejudice or disclaimer; and claims 45-48 have been added. The amendments and new claims add no new matter and are fully supported by the specification and claims as filed as discussed below. Upon entry of the present amendment, claims 2, 19 and 45-48 will be pending in this application.

Claim Amendments and New Claims

Claim 1 has been amended to recite the limitations of canceled claims 9 and 10. Support for the amendment may be found in original claims 9 and 10. As such, no new matter is introduced by the amendment and entry of the amendment is respectfully requested.

Support for new claim 45 may be found throughout the specification and claims as filed, for example, on page 13, line 29 (WO2004/065932). As such, no new matter is introduced by addition of new claim 8 and entry of the claim is respectfully requested.

Support for new claim 46 may be found throughout the specification and claims as filed, for example, on page 48, lines 6-15 (WO2004/065932). As such, no new matter is introduced by addition of new claim 8 and entry of the claim is respectfully requested.

Support for new claim 47 may be found throughout the specification and claims as filed, for example, on page 41, lines 18-28 and page 42, lines 4-14 (WO2004/065932). As such, no new matter is introduced by addition of new claim 8 and entry of the claim is respectfully requested.

Support for new claim 48 may be found throughout the specification and claims as filed, for example, on page 15, lines 7-20 and page 15, line 21 to page 16, line 17 (WO2004/065932). As such, no new matter is introduced by addition of new claim 8 and entry of the claim is respectfully requested.

Rejection under 35 U.S.C. §35 U.S.C. §102

Applicants respectfully traverse the rejection of claim 2 under 35 U.S.C. §102(a) as allegedly being anticipated by Ruggiero et al. (*Society for Neuroscience,* Prog. No. 441.11, Abstract (2002); hereinafter 'Ruggiero').

To anticipate, a single reference must inherently or expressly teach each and every element of the claimed invention (*see, In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); and MPEP § 2131).

The Office Action alleges that Ruggiero discloses a method including contacting a cell expressing GTRAP3-18 with a test compound, and determining the glycosylation level of EAAT glutamate transporters. Without acquiescing to the rationale provided in the Office Action, claim 2 has been amended to recite that the GTRAP3-18 target molecule is glutamate transporter GLAST/EAAT1. The cited reference fails to disclose a method utilizing the glutamate transporter GLAST/EAAT1 as currently claimed. As such, Ruggiero fails to teach each and every element of the claims and therefore fails to anticipate the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. §35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 2, 9 , 10 and 19 under 35 U.S.C. §103 as allegedly obvious over Lin et al. (*Nature,* 410:84-88 (2001); hereinafter 'Lin'), in view of Trotti et al. (*Journal of Biological Chemistry,* 276(1):576-582 (2001); hereinafter 'Trotti').

The U.S. Supreme Court decision in *KSR International v. Teleflex Inc.* (82 USPQ 2d 1385), modified the standard for establishing a prima facie case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the

general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The new Guidelines establishing standards for obviousness emphasize that Examiners "must provide a reasoned explanation as to why the invention as claimed would have been obvious," and are equally clear that "familiar lines of argument," *e.g.*, a showing of unexpected results, a lack of reasonable expectation of success, and a teaching away from the claimed invention by the prior art, can still demonstrate the nonobviousness of a claimed invention. Applicants submit that the Examiner has not met the burden of establishing a *prime facie* case of nonobviousness for the reasons discussed below.

As discussed above, claim 2 has been amended to recite that the GTRAP3-18 target molecule is GLAST/EAAT1. As such, the claims are drawn to a method for identifying a compound which modulates cellular glycosylation, comprising: a) contacting a cell which expresses GTRAP3-18 with a test compound; and b) identifying the test compound as a modulator of cellular glycosylation by assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, thereby identifying a compound which modulates cellular glycosylation, wherein the GTRAP3-18 target molecule is glutamate transporter GLAST/EAAT1.

The Office Action cites Lin as allegedly disclosing contacting cells expressing GTRAP3-18 with test compounds and assaying the ability of the test compounds to modulate GTRAP3-18 protein expression. The Office Action further alleges that Lin discloses a specific protein-protein interaction between GTRAP3-18 and certain EAATs, thus identifying these glutamate transporters as GTRAP3-18 target molecules. However, as regards the claims as amended, Lin is silent as to a method including detecting the level of glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is the glutamate transporter GLAST/EAAT1. As such, the reference fail to disclose each and every element of the claimed invention.

The Office Action cites Trotti as allegedly disclosing that it was well known in the art that EAAT transporters affect glutamate clearance activity. To this point, the Office Action alleges that Trotti discloses methods that include detecting the level of glycosylation of the glutamate transporter GLT1 (also known as EAAT2). However, as regards the claims as amended, Trotti is silent as to a method including detecting the level of glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is the glutamate transporter GLAST/EAAT1. As such, the reference fail to disclose each and every element of the claimed invention. Since Lin and Trotti fail to disclose each and every element of the claims as amended, no *prima facie* case of obviousness has been established.

Further, Applicants assert that the Office Action fails to establish a *prima facie* case of obviousness because the cited references provide no motivation to modify the references or combine the references to arrive at the claimed invention. The Office Action acknowledges that Lin fails to teach a method which includes detecting the level of glycosylation of a GRTAP3-18 target molecule as claimed. However, the Office Action attempts to remedy the deficiencies of Lin with Trotti. As discussed above, Trotti allegedly discloses a method including detecting the level of glycosylation of glutamate transporter GLT1 (also known as EAAT2).

Applicants assert that no motivation is provided to combine the references to arrive at the claimed method which includes detecting glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is glutamate transporter GLAST/EAAT1. The Office Action asserts that Lin discloses a specific protein-protein interaction between GTRAP3-18 and certain EAATs, thus identifying glutamate transporters as GTRAP3-18 target molecules. However, Lin discloses that no such interaction exists between GTRAP3-18 and glutamate transporter GLAST/EAAT1 (see Figure 1 of Lin). This observation would lead one of skill in the art to conclude that the glutamate transporter GLAST/EAAT1 is not a GTRAP3-18 target molecule and therefore provides no motivation to detect glycosylation of GLAST/EAAT1 as claimed. Further, Trotti relates to GLT1 (also known as EAAT2) and is silent as to a method including detecting the level of glycosylation of glutamate transporter GLAST/EAAT1 and therefore provides no motivation to detect glycosylation of GLAST/EAAT1. Additionally, both Lin and Trotti fail to

disclose a correlation between GTRAP3-18 activity regulation or expression and general modulation of cellular glycosylation as claimed. The references provide no suggestion or guidance as to a potential role of GTRAP3-18 in modulating general cellular glycosylation.

It is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim (*see, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985)). As the references combined do not teach all of the elements of the present claims, nor is there provided a suggestion or motivation to combine the references, no *prima facie* case of obviousness has been established. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants respectfully traverse the rejection of claims 2, 9, 10 and 19 under 35 U.S.C. §103 as allegedly obvious over U.S. Patent No. 6,808,893 (Rothstein et al., hereinafter 'the '893 Patent'), further in view of Trotti.

Applicants assert that the Office Action fails to establish a *prima facie* case of obviousness because the cited references fail to disclose each and every element of the claimed invention. As discussed above, claim 2 has been amended to recite that the GTRAP3-18 target molecule is GLAST/EAAT1. The Office Action cites the '893 Patent as allegedly disclosing contacting cells expressing GTRAP3-18 with test compounds and assaying the ability of the test compounds to modulate GTRAP3-18 protein expression. However, as regards the claims as amended, the '893 Patent is silent as to a method including detecting the level of glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is the glutamate transporter GLAST/EAAT1. As such, the reference fail to disclose each and every element of the claimed invention.

The Office Action cites Trotti as allegedly disclosing methods for detecting the level of glycosylation of EAAT transporters. However, as regards the claims as amended, Trotti is silent as to a method including detecting the level of glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is the glutamate transporter GLAST/EAAT1. As such, the reference fail to disclose each and every element of the claimed invention. Since the '893 Patent and Trotti

fail to disclose each and every element of the claims as amended, no *prima facie* case of obviousness has been established.

Further, Applicants assert that the Office Action fails to establish a *prima facie* case of obviousness because the cited references provide no motivation to modify the references or combine the references to arrive at the claimed invention. The Office Action acknowledges that the '893 Patent fails to teach a method which includes detecting the level of glycosylation of a GRTAP3-18 target molecule as claimed. The Office Action attempts to remedy the deficiencies of the '893 Patent with Trotti. As discussed above, Trotti allegedly discloses methods of detecting the level of glycosylation of EAAT transporters. However, no motivation exists to combine the references to arrive at the claimed method which includes detecting glycosylation of a GTRAP3-18 target molecule, wherein the target molecule is glutamate transporter GLAST/EAAT1. Both the '893 Patent and Trotti are silent as to a method including detecting the level of glycosylation of glutamate transporter GLAST/EAAT1 and therefore provide no motivation to detect glycosylation of GLAST/EAAT1 as claimed.

As the references combined do not teach all of the elements of the present claims, nor is there provided a suggestion or motivation to combine the references, no *prima facie* case of obviousness has been established. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Commissioner is hereby authorized to charge the total amount of $470.00 to cover the payment of a Request for Continued Examination fee ($405.00) and a One-Month Extension of Time fee ($65.00), small entity, to Deposit Account No. 07-1896. No other fees are deemed necessary with the filing of this paper. However, if any additional fees are due, the Commissioner is further authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

Date: October 5, 2010

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